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* STN Columbus *

FILE 'HOME' ENTERED AT 10:59:12 ON 27 APR 2004

=> FIL STNGUIDE
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|
| 0.21 | 0.21 |

FILE 'STNGUIDE' ENTERED AT 10:59:22 ON 27 APR 2004

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 23, 2004 (20040423/UP).

| | | | |
|----------------------|--|------------|---------|
| => FIL HOME | | SINCE FILE | TOTAL |
| COST IN U.S. DOLLARS | | ENTRY | SESSION |
| FULL ESTIMATED COST | | 0.06 | 0.27 |

FILE 'HOME' ENTERED AT 10:59:25 ON 27 APR 2004

| | | | |
|----------------------|--|------------|---------|
| => fil reg | | SINCE FILE | TOTAL |
| COST IN U.S. DOLLARS | | ENTRY | SESSION |
| FULL ESTIMATED COST | | 0.21 | 0.48 |

FILE 'REGISTRY' ENTERED AT 10:59:32 ON 27 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7
DICTIONARY FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

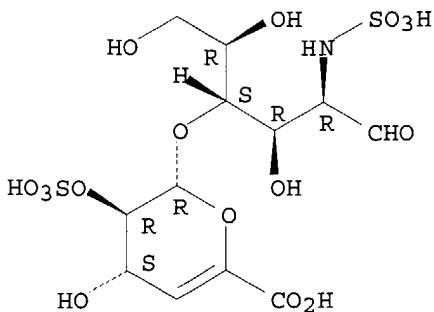
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s 136098-03-8
L1 1 136098-03-8
(136098-03-8/RN)

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 136098-03-8 REGISTRY
CN D-Glucose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo- α -L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, trisodium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C12 H19 N O16 S2 . 3 Na
SR CAS Client Services
LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM, TOXCENTER, USPATFULL
CRN (53695-16-2)

Absolute stereochemistry.



●3 Na

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil medl caplu biosis uspatf wpid

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

2.61

3.09

FILE 'MEDLINE' ENTERED AT 11:00:27 ON 27 APR 2004

FILE 'CAPLUS' ENTERED AT 11:00:27 ON 27 APR 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE 'BIOSIS' ENTERED AT 11:00:27 ON 27 APR 2004

COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC. (R)

FILE 'USPATFULL' ENTERED AT 11:00:27 ON 27 APR 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 11:00:27 ON 27 APR 2004

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=> s l1

L2 4 L1

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 4 DUP REM L2 (0 DUPLICATES REMOVED)

=> d ibib abs tot

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:454053 CAPLUS

DOCUMENT NUMBER: 139:30781

TITLE: Heparin- and heparan sulfate-derived oligosaccharide metastasis-blocking anticancer compounds

INVENTOR(S): Cahalon, Liora; Cohen, Irun R.; Lider, Ofer; Margalit, Raanan

PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|------------|
| WO 2003047501 | A2 | 20030612 | WO 2002-IL982 | 20021205 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2003130230 | A1 | 20030710 | US 2001-2145 | 20011205 |
| PRIORITY APPLN. INFO.: | | | US 2001-2145 | A 20011205 |

OTHER SOURCE(S) : MARPAT 139:30781

AB The invention discloses a treatment for cancer, and in particular, therapeutic compds. which block the ability of cytokines and chemokines to promote metastasis of malignant cells. The therapeutic compds. comprise a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan sulfate-derived saccharide compound. In one embodiment, the carbohydrate or oligosaccharide has a mol. weight of no more than about 3000 daltons, preferably in the range of about 400-2000 daltons, most preferably between about 400-1100 daltons. Generally, substances of the invention inhibit tumor cell migration, as determined by biol. assays, and comprise mols. of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

L3 ANSWER 2 OF 4 USPATFULL on STN

ACCESSION NUMBER: 2003:188437 USPATFULL
 TITLE: Novel anti-cancer therapeutic compounds
 INVENTOR(S) : Cahalon, Liora, Givataim, ISRAEL
 Cohen, Irun R., Rehovot, ISRAEL
 Lider, Ofer, Kfar Bilu Bet, ISRAEL
 Margalit, Raanan, Ganei Yochanan, ISRAEL

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003130230 | A1 | 20030710 |
| APPLICATION INFO.: | US 2001-2145 | A1 | 20011205 (10) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | C/O THE POLKINGHORNS, 9003 FLORIN WAY, UPPER MARLBORO, MD, 20772 | | |
| NUMBER OF CLAIMS: | 32 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 15 Drawing Page(s) | | |
| LINE COUNT: | 940 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A treatment for cancer, and in particular, of therapeutic compounds which block the ability of cytokines and chemokines to promote metastasis of malignant cells. The therapeutic compound comprises a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan-sulfate derived saccharide compound. In one embodiment of the present invention, the carbohydrate or oligosaccharide has a molecular weight of no more than about 3000 daltons, preferably lying in the range of about 400 to about 2000 daltons, most preferably between about 400 and about 1100 daltons. Generally, substances of the present invention inhibit tumor

cell migration, as determined by biological assays, and comprise molecules of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:116287 CAPLUS
DOCUMENT NUMBER: 139:334949
TITLE: Retention studies of sulphated glycosaminoglycan disaccharides on porous graphitic carbon capillary columns
AUTHOR(S): Koivisto, P.; Stefansson, M.
CORPORATE SOURCE: Uppsala Research Imaging Solution AB, Uppsala, 75185, Swed.
SOURCE: Chromatographia (2003), 57(1/2), 37-45
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The retention behavior of highly polar and charged disaccharide isomers has been studied on porous graphitic carbon columns and exptl. parameters were varied over wide a range, including concentration and type of mobile phase constituents as well as temperature. The hydrophilic and anionic sugar analytes were highly retained on this stationary phase compared to the octadecyl-derivatized silica packings more commonly used. E.g., an increase in retention with polarity of a solute and with temperature was observed

By isotherm measurements and nonlinear fitting of Langmuirian expressions to the exptl. data the graphite surface appeared homogeneous with only one kind of active adsorption site for these kinds of compound which was furthermore supported by the linear Van't Hoff plots obtained by varying the temperature. The gain in free energy was found to be entropically driven after determination of the ΔH° and ΔS° values. However, enthalpy-entropy compensation behavior was not met.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:136668 CAPLUS
DOCUMENT NUMBER: 135:256060
TITLE: Disaccharides derived from heparin or heparan sulfate regulate IL-8 and IL-1 β secretion by intestinal epithelial cells
AUTHOR(S): Chowers, Yehuda; Lider, Ofer; Schor, Hagai; Barshack, Iris; Tal, Ruth; Ariel, Amiram; Bar-Meir, Simon; Cohen, Irun R.; Cahalon, Liora
CORPORATE SOURCE: Departments of Gastroenterology, Chaim Sheba Medical Center, Tel-HaShomer, Israel
SOURCE: Gastroenterology (2001), 120(2), 449-459
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background & Aims: Intestinal epithelial cells can produce cytokines and chemokines that play an important role in the mucosal immune response. Regulation of this secretion is important to prevent inflammatory tissue damage. Disaccharides derived from heparan sulfate and heparin have been shown to down-regulate inflammation in vivo. We tested the effect of such disaccharides on cytokine secretion by intestinal epithelial cells. Methods: Spontaneous and tumor necrosis factor (TNF)- α -stimulated interleukin (IL)-8 and IL-1 β secretion and mRNA expression were assessed in HT-29 and Caco-2 intestinal epithelial cell lines in the

presence of a panel of heparin and heparan sulfate disaccharides. Results: Specific disaccharides suppressed spontaneous and TNF- α -induced mediator secretion in a dose-dependent manner. Disaccharide activity was structurally restricted. Preincubation of cells with nonsuppressing disaccharides blocked the activity of suppressing disaccharides. The number of sulfate moieties determined the ability of nonsuppressing disaccharides to block the effect of suppressive disaccharides. No suppression of mRNA expression was noted, and intracellular mediator levels were not reduced. Conclusions: Disaccharides derived from heparin and heparan sulfate regulate proinflammatory mediator secretion from intestinal epithelial cells. Dose dependence and competition by structurally diverging disaccharides suggest a receptor-mediated mechanism. Unchanged mRNA and intracellular mediator levels suggest that the disaccharides act at posttranscriptional stages.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

| | | | |
|--|------------|---------|--|
| => fil reg | | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| FULL ESTIMATED COST | 16.76 | 19.85 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| CA SUBSCRIBER PRICE | -2.08 | -2.08 | |

FILE 'REGISTRY' ENTERED AT 11:02:55 ON 27 APR 2004
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STRUCTURE FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7
DICTIONARY FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

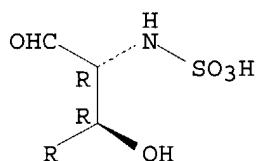
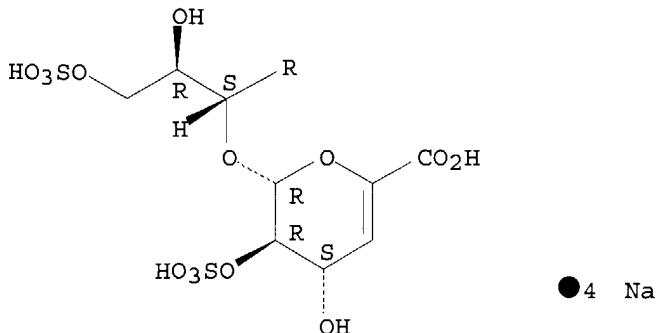
=> s 136098-10-7
L4 1 136098-10-7
(136098-10-7/RN)

=> d

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 136098-10-7 REGISTRY
CN D-Glucose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo- α -L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C12 H19 N O19 S3 . 4 Na
SR CAS Client Services
LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM, TOXCENTER, USPAT2, USPATFULL

CRN (53860-65-4)

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FIL MEDL CAPLU BIOSIS USPATF WPID

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

2.19

22.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY

TOTAL
SESSION

CA SUBSCRIBER PRICE

0.00

-2.08

FILE 'MEDLINE' ENTERED AT 11:03:20 ON 27 APR 2004

FILE 'CAPLUS' ENTERED AT 11:03:20 ON 27 APR 2004

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FILE 'BIOSIS' ENTERED AT 11:03:20 ON 27 APR 2004

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FILE 'USPATFULL' ENTERED AT 11:03:20 ON 27 APR 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 11:03:20 ON 27 APR 2004

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=> s 14

L5 9 L4

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 9 DUP REM L5 (0 DUPLICATES REMOVED)

=> d ibib abs tot

L6 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:454053 CAPLUS
 DOCUMENT NUMBER: 139:30781
 TITLE: Heparin- and heparan sulfate-derived oligosaccharide metastasis-blocking anticancer compounds
 INVENTOR(S): Cahalon, Liora; Cohen, Irun R.; Lider, Ofer; Margalit, Raanan
 PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2003047501 | A2 | 20030612 | WO 2002-IL982 | 20021205 |
| W: | AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2003130230 | A1 | 20030710 | US 2001-2145 | 20011205 |
| PRIORITY APPLN. INFO.: | | | US 2001-2145 | A 20011205 |

OTHER SOURCE(S): MARPAT 139:30781

AB The invention discloses a treatment for cancer, and in particular, therapeutic compds. which block the ability of cytokines and chemokines to promote metastasis of malignant cells. The therapeutic compds. comprise a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan sulfate-derived saccharide compound. In one embodiment, the carbohydrate or oligosaccharide has a mol. weight of no more than about 3000 daltons, preferably in the range of about 400-2000 daltons, most preferably between about 400-1100 daltons. Generally, substances of the invention inhibit tumor cell migration, as determined by biol. assays, and comprise mols. of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

L6 ANSWER 2 OF 9 USPATFULL on STN
 ACCESSION NUMBER: 2003:188437 USPATFULL
 TITLE: Novel anti-cancer therapeutic compounds
 INVENTOR(S): Cahalon, Liora, Givataim, ISRAEL
 Cohen, Irun R., Rehovot, ISRAEL
 Lider, Ofer, Kfar Bilu Bet, ISRAEL
 Margalit, Raanan, Ganei Yochanan, ISRAEL

| PATENT INFORMATION: | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| APPLICATION INFO.: | US 2003130230 | A1 | 20030710 |
| DOCUMENT TYPE: | US 2001-2145 | A1 | 20011205 (10) |
| FILE SEGMENT: | Utility | | |
| LEGAL REPRESENTATIVE: | C/O THE POLKINGHORNS, 9003 FLORIN WAY, UPPER MARLBORO, MD, 20772 | | |
| NUMBER OF CLAIMS: | 32 | | |

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 940

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A treatment for cancer, and in particular, of therapeutic compounds which block the ability of cytokines and chemokines to promote metastasis of malignant cells. The therapeutic compound comprises a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan-sulfate derived saccharide compound. In one embodiment of the present invention, the carbohydrate or oligosaccharide has a molecular weight of no more than about 3000 daltons, preferably lying in the range of about 400 to about 2000 daltons, most preferably between about 400 and about 1100 daltons. Generally, substances of the present invention inhibit tumor cell migration, as determined by biological assays, and comprise molecules of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:116287 CAPLUS
DOCUMENT NUMBER: 139:334949
TITLE: Retention studies of sulphated glycosaminoglycan disaccharides on porous graphitic carbon capillary columns
AUTHOR(S): Koivisto, P.; Stefansson, M.
CORPORATE SOURCE: Uppsala Research Imaging Solution AB, Uppsala, 75185, Swed.
SOURCE: Chromatographia (2003), 57(1/2), 37-45
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The retention behavior of highly polar and charged disaccharide isomers has been studied on porous graphitic carbon columns and exptl. parameters were varied over wide a range, including concentration and type of mobile phase constituents as well as temperature. The hydrophilic and anionic sugar analytes were highly retained on this stationary phase compared to the octadecyl-derivatized silica packings more commonly used. E.g., an increase in retention with polarity of a solute and with temperature was observed

By isotherm measurements and nonlinear fitting of Langmuirian expressions to the exptl. data the graphite surface appeared homogeneous with only one kind of active adsorption site for these kinds of compound which was furthermore supported by the linear Van't Hoff plots obtained by varying the temperature. The gain in free energy was found to be entropically driven after determination of the ΔH° and ΔS° values. However, enthalpy-entropy compensation behavior was not met.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2002:32546 USPATFULL
TITLE: Pharmaceutical compositions containing oligosaccharides, the novel oligosaccharides and preparation thereof
INVENTOR(S): Mourier, Pierre, Charenton Le Pont, FRANCE
Perrin, Elisabeth, Evreux, FRANCE
Viskov, Christian, Ris Orangis, FRANCE

| NUMBER | KIND | DATE |
|--------|-------|-------|
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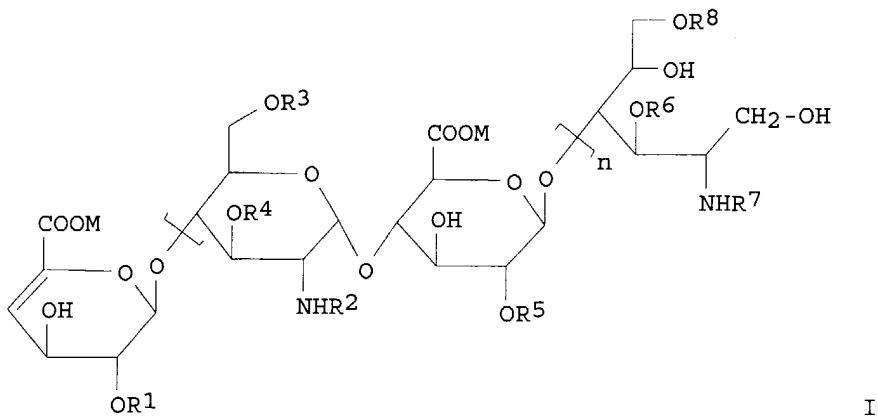
PATENT INFORMATION: US 2002019368 A1 20020214
 US 6608042 B2 20030819
 APPLICATION INFO.: US 2001-817428 A1 20010326 (9)

| | NUMBER | DATE |
|--|--|---------------|
| ----- | | |
| PRIORITY INFORMATION: | FR 2000-3910 | 20000328 |
| | US 2000-205026P | 20000518 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | AVENTIS PHARMACEUTICALS, INC., PATENTS DEPARTMENT, ROUTE 202-206, P.O. BOX 6800, BRIDGEWATER, NJ, 08807-0800 | |
| NUMBER OF CLAIMS: | 36 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 983 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |
| AB | The present invention relates to pharmaceutical compositions containing as an active ingredient at least one oligosaccharide of formula: ##STR1## | |
| | to novel oligosaccharides of formula (I), to mixtures thereof and to methods for their preparation. | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:730755 CAPLUS
 DOCUMENT NUMBER: 135:273169
 TITLE: Preparation of uronic acid-containing oligosaccharides as antiinflammatory agents
 INVENTOR(S): Mourier, Pierre; Perrin, Elisabeth; Viskov, Christian
 PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|-------------------|----------|-----------------|------------|
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| WO 2001072762 | A1 | 20011004 | WO 2001-FR903 | 20010326 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| FR 2807043 | A1 | 20011005 | FR 2000-3910 | 20000328 |
| FR 2807043 | B1 | 20021122 | | |
| US 2002019368 | A1 | 20020214 | US 2001-817428 | 20010326 |
| US 6608042 | B2 | 20030819 | | |
| EP 1272499 | A1 | 20030108 | EP 2001-919561 | 20010326 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001009617 | A | 20030204 | BR 2001-9617 | 20010326 |
| JP 2003529570 | T2 | 20031007 | JP 2001-570671 | 20010326 |
| NO 2002004590 | A | 20020925 | NO 2002-4590 | 20020925 |
| PRIORITY APPLN. INFO.: | | | FR 2000-3910 | A 20000328 |
| | | | WO 2001-FR903 | W 20010326 |
| OTHER SOURCE(S): | MARPAT 135:273169 | | | |



AB Uronic acid-containing oligosaccharides I ($n = 0-25$; R1, R3-R6, R8 are independently H, SO₃M; R2, R7 independently H, SO₃M, COMe; M is Na, Ca, Mg, K, oligosaccharide) were prepared from heparin as antiinflammatory agents. Thus, I ($n = 1$; R1-R3 = R5 = R7-R8 = SO₃Na; R4 = R6 = H) was prepared and tested in mice as antiinflammatory agent.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:136668 CAPLUS

DOCUMENT NUMBER: 135:256060

TITLE: Disaccharides derived from heparan sulfate regulate IL-8 and IL-1 β secretion by intestinal epithelial cells

AUTHOR(S): Chowers, Yehuda; Lider, Ofer; Schor, Hagai; Barshack, Iris; Tal, Ruth; Ariel, Amiram; Bar-Meir, Simon; Cohen, Irun R.; Cahalon, Liora

CORPORATE SOURCE: Departments of Gastroenterology, Chaim Sheba Medical Center, Tel-HaShomer, Israel

SOURCE: Gastroenterology (2001), 120(2), 449-459
CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background & Aims: Intestinal epithelial cells can produce cytokines and chemokines that play an important role in the mucosal immune response. Regulation of this secretion is important to prevent inflammatory tissue damage. Disaccharides derived from heparan sulfate and heparin have been shown to down-regulate inflammation in vivo. We tested the effect of such disaccharides on cytokine secretion by intestinal epithelial cells.

Methods: Spontaneous and tumor necrosis factor (TNF)- α -stimulated interleukin (IL)-8 and IL-1 β secretion and mRNA expression were assessed in HT-29 and Caco-2 intestinal epithelial cell lines in the presence of a panel of heparin and heparan sulfate disaccharides.

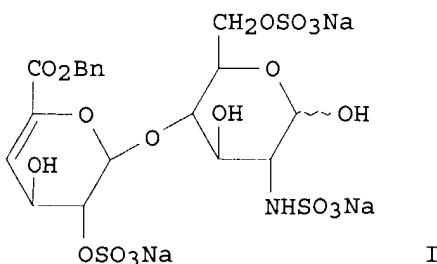
Results: Specific disaccharides suppressed spontaneous and TNF- α -induced mediator secretion in a dose-dependent manner.

Disaccharide activity was structurally restricted. Preincubation of cells with nonsuppressing disaccharides blocked the activity of suppressive disaccharides. The number of sulfate moieties determined the ability of nonsuppressing disaccharides to block the effect of suppressive disaccharides. No suppression of mRNA expression was noted, and intracellular mediator levels were not reduced. Conclusions: Disaccharides derived from heparin and heparan sulfate regulate proinflammatory mediator secretion from intestinal epithelial cells. Dose

dependence and competition by structurally diverging disaccharides suggest a receptor-mediated mechanism. Unchanged mRNA and intracellular mediator levels suggest that the disaccharides act at posttranscriptional stages.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:114405 CAPLUS
DOCUMENT NUMBER: 124:250216
TITLE: Synthesis and biological activity of a model disaccharide containing a key unit in heparin for binding to platelets
AUTHOR(S): Suda, Yasuo; Bird, Karyn; Shiyama, Takaaki; Koshida, Shuhei; Marques, Dalila; Fukase, Koichi; Sobel, Michael; Kusumoto, Shoichi
CORPORATE SOURCE: Dep. Chem., Osaka Univ., Toyonaka, 560, Japan
SOURCE: Tetrahedron Letters (1996), 37(7), 1053-6
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To determine the specific site(s) in heparin necessary for binding to platelets, synthesis of a model compound containing the disaccharide sequence, O-(2-deoxy-2-sulfamido-6-O-sulfo- α -D-glucopyranosyl)-(1 \rightarrow 4)-2-O-sulfo- α -L-idopyranuronic acid, found in heparin was performed by α -selective glycosidation using a Ph thioglycoside as a donor. The compound inhibited 125 I-labeled heparin binding to human platelets to a greater extent than a heparin-derived disaccharide, obtained by the heparinase I digestion, yet contained the same number of sulfate groups per mol.

L6 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:352418 CAPLUS
DOCUMENT NUMBER: 122:240283
TITLE: Capillary electrophoresis for monitoring chemical reactions: sulfation and synthetic manipulation of sulfated carbohydrates
AUTHOR(S): Kerns, Robert J.; Vlahov, Ioncho R.; Linhardt, Robert J.
CORPORATE SOURCE: Division of Medicinal and Natural Products, Chemistry, College of Pharmacy, University of Iowa, Iowa City, IA 52242, USA
SOURCE: Carbohydrate Research (1995), 267(1), 143-52
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The use of capillary electrophoresis as an anal. tool for monitoring chemical reactions of sulfated disaccharides, e.g. I, is described.

L6 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:421203 CAPLUS
 DOCUMENT NUMBER: 123:33561
 TITLE: Preparation and structural characterization of large
 heparin-derived oligosaccharides
 AUTHOR(S): Pervin, Azra; Gallo, Cindy; Jandik, Kenneth A.; Han,
 Xue-Jun; Linhardt, Robert J.
 CORPORATE SOURCE: Coll. Pharmacy, Univ. Iowa, Iowa City, IA, 52242, USA
 SOURCE: Glycobiology (1995), 5(1), 83-95
 CODEN: GLYCE3; ISSN: 0959-6658
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Porcine mucosal heparin was partially depolymerized with heparin lyase I and
 then fractionated into low-mol.-weight (<5000) and high-mol.-weight (>5000)
 oligosaccharides by pressure filtration. The high-mol.-weight
 oligosaccharide mixture (.apprx.50 wt% of the starting heparin) also
 contained intact heparin. This intact polymer complicates oligosaccharide
 purification. Thus, the low-mol.-weight fraction was used to prepare
 homogeneous
 oligosaccharides for structural characterization. The low-mol.-weight
 oligosaccharide mixture was first fractionated by low-pressure gel
 permeation chromatog. into size-uniform mixts. of disaccharides,
 tetrasaccharides, hexasaccharides, octasaccharides, decasaccharides,
 dodecasaccharides, tetradecasaccharides and higher oligosaccharides. Each
 size-fractionated mixture was then purified on the basis of charge by
 repetitive semi-preparative strong-anion-exchange HPLC. This approach has
 led to the isolation of 14 homogeneous oligosaccharides from disaccharide
 to tetradecasaccharide. The structure of these oligosaccharides was
 established using 600 MHz two-dimensional nuclear resonance spectroscopy.
 The utility of two-dimensional nuclear resonance spectroscopy to determine the
 structure of complex heparin oligosaccharides is also illustrated.

=> FIL STNGUIDE

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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Apr 23, 2004 (20040423/UP).

=> fil capl

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|--|------------------|---------------|
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| CA SUBSCRIBER PRICE | 0.00 | -6.93 |

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FILE COVERS 1907 - 27 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 26 Apr 2004 (20040426/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 6020323/pn
L7 0 6020323/PN

=> s us6020323/pn
L8 1 US6020323/PN

=> d

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:517701 CAPLUS
DN 121:117701
TI Oligosaccharides for the regulation of cytokine activity
IN Cohen, Irun R.; Lider, Ofer; Cahalon, Liora; Shoseyov, Oded; Margalit, Raanan
PA Yeda Research and Development Co. Ltd., Israel
SO PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| PI | WO 9411006 | A1 | 19940526 | WO 1993-US10868 | 19931109 |
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| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2149116 | AA | 19940526 | CA 1993-2149116 | 19931109 |
| | AU 9455993 | A1 | 19940608 | AU 1994-55993 | 19931109 |
| | AU 686581 | B2 | 19980212 | | |
| | EP 669827 | A1 | 19950906 | EP 1994-901394 | 19931109 |
| | EP 669827 | B1 | 20010523 | | |
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| | HU 70945 | A2 | 19951128 | HU 1995-1373 | 19931109 |
| | JP 08506322 | T2 | 19960709 | JP 1994-512329 | 19931109 |
| | EP 1095657 | A2 | 20010502 | EP 2000-123134 | 19931109 |
| | EP 1095657 | A3 | 20040225 | | |
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| | CN 1093904 | A | 19941026 | CN 1993-121328 | 19931110 |
| | NO 9501822 | A | 19950629 | NO 1995-1822 | 19950509 |
| | FI 9502267 | A | 19950710 | FI 1995-2267 | 19950510 |
| | US 6020323 | A | 20000201 | US 1995-486127 | 19950607 <-- |
| | US 5861382 | A | 19990119 | US 1995-436330 | 19950629 |
| | AU 9864783 | A1 | 19980625 | AU 1998-64783 | 19980508 |
| | AU 699624 | B2 | 19981210 | | |

PRAI US 1992-974750 A 19921110
US 1993-96739 A 19930723
US 1992-878188 B2 19920501
EP 1994-901394 A3 19931109
WO 1993-US10868 W 19931109
US 1995-384203 A1 19950203
US 1995-436330 A1 19950510

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E1 THROUGH E11 ASSIGNED

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FULL ESTIMATED COST 5.22 56.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
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CA SUBSCRIBER PRICE 0.00 -6.93

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STRUCTURE FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7
DICTIONARY FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Experimental and calculated property data are now available. For more
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<http://www.cas.org/ONLINE/DBSS/registryss.html>

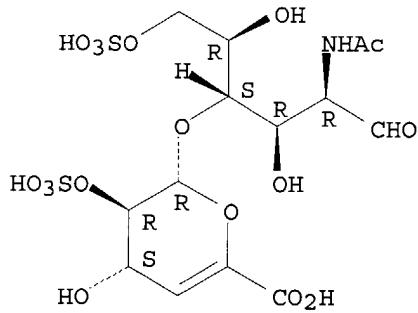
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=> d scan

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Absolute stereochemistry.

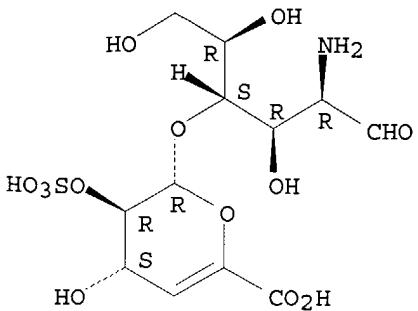


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L9 11 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
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 MF C12 H19 N O13 S
 CI COM

Absolute stereochemistry.

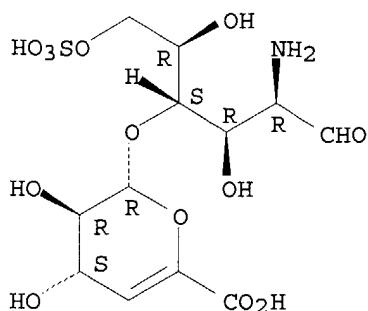


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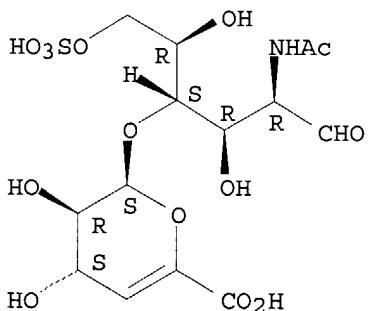
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MF C14 H21 N O14 S

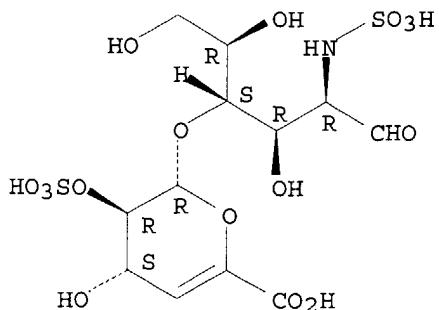
Absolute stereochemistry.



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MF C12 H19 N O16 S2
CI COM

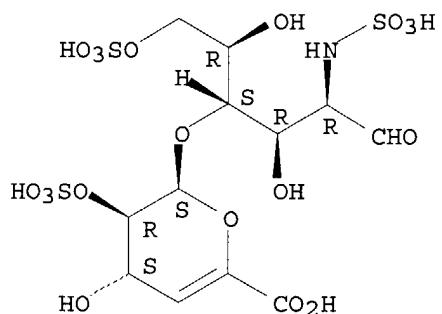
Absolute stereochemistry.



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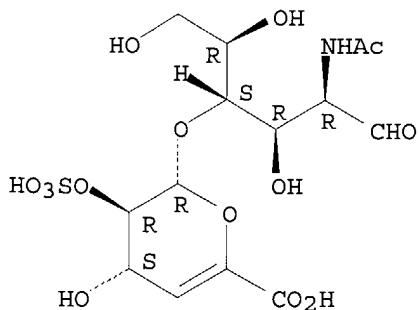
Absolute stereochemistry.



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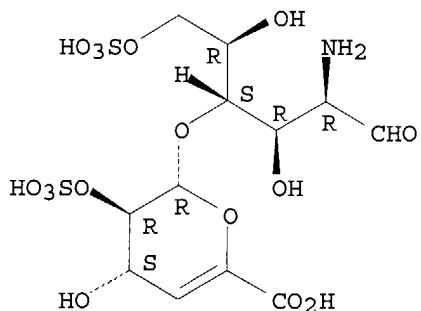
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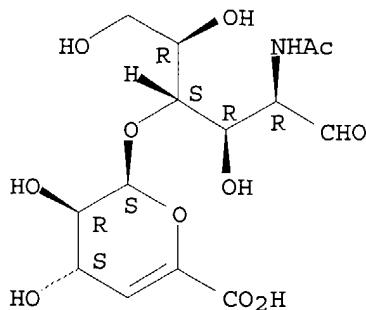
Absolute stereochemistry.



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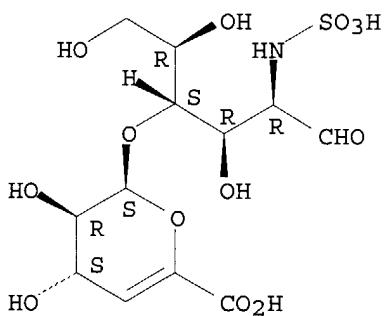
Absolute stereochemistry.



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 IN D-Glucose, 2-deoxy-4-O-(4-deoxy-beta-L-threo-hex-4-enopyranuronosyl)-2-
 (sulfoamino)- (9CI)
 MF C12 H19 N O13 S

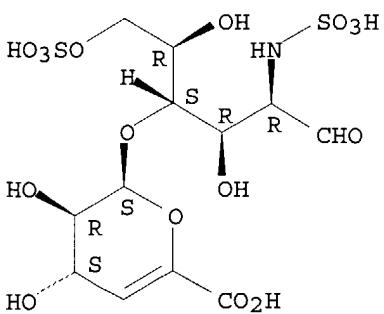
Absolute stereochemistry.



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 IN D-Glucose, 2-deoxy-4-O-(4-deoxy-beta-L-threo-hex-4-enopyranuronosyl)-2-
 (sulfoamino)-, 6-(hydrogen sulfate) (9CI)
 MF C12 H19 N O16 S2

Absolute stereochemistry.



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ALL ANSWERS HAVE BEEN SCANNED

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| CA SUBSCRIBER PRICE | | ENTRY | SESSION |
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| => FIL MEDL CAPLU BIOSIS USPATF WPID | | SINCE FILE | TOTAL |
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FILE 'WPIDS' ENTERED AT 11:18:53 ON 27 APR 2004
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=> s heparin sulfate disaccharide
L10 4 HEPARIN SULFATE DISACCHARIDE

=> s heparin sulfate disaccharides
L11 0 HEPARIN SULFATE DISACCHARIDES

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PROCESSING COMPLETED FOR L10
L12 4 DUP REM L10 (0 DUPLICATES REMOVED)

=> d ibib abs tot

L12 ANSWER 1 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2003:324286 USPATFULL
TITLE: Measurement of biosynthesis and breakdown rates of

biological molecules that are inaccessible or not easily accessible to direct sampling, non-invasively, by label incorporation into metabolic derivatives and catabolic products

INVENTOR(S) : Hellerstein, Marc K., Kensington, CA, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003228259 | A1 | 20031211 |
| APPLICATION INFO.: | US 2003-366125 | A1 | 20030212 (10) |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2002-356008P | 20020212 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | MORRISON & FOERSTER LLP, 425 MARKET STREET, SAN FRANCISCO, CA, 94105-2482 | |
| NUMBER OF CLAIMS: | 59 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 14 Drawing Page(s) | |
| LINE COUNT: | 3036 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of determining rate of biosynthesis or breakdown of biological molecules from metabolic derivatives and catabolic products are disclosed herein. In particular, methods of measuring the rates of biosynthesis and breakdown of biological molecules inaccessible or not easily accessible to direct sampling by sampling metabolic derivatives and catabolic products in accessible biological samples are disclosed herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 4 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-689661 [65] WPIDS
DOC. NO. CPI: C2003-189144
TITLE: Determining rate of biosynthesis or breakdown of inaccessible biological molecules, useful e.g. for diagnosis or monitoring treatment, by administering labeled precursor.
DERWENT CLASS: B04 D16 K08
INVENTOR(S) : HELLERSTEIN, M K
PATENT ASSIGNEE(S) : (HELL-I) HELLERSTEIN M K; (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 102
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|------|--------------------|------|-----|----|
| WO 2003068919 | A2 | 20030821 (200365)* | EN | 105 | |
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| US 2003228259 | A1 | 20031211 (200382) | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|----------------|-----------------|----------|
| WO 2003068919 | A2 | WO 2003-US4183 | 20030212 |
| US 2003228259 | A1 Provisional | US 2002-356008P | 20020212 |
| | | US 2003-366125 | 20030212 |

PRIORITY APPLN. INFO: US 2002-356008P 20020212; US
2003-366125 20030212

AN 2003-689661 [65] WPIDS

AB WO2003068919 A UPAB: 20031009

NOVELTY - Determining the rate of biosynthesis or breakdown of at least one inaccessible biological molecule (I) in a subject, is new.

DETAILED DESCRIPTION - Determining the rate of biosynthesis or breakdown of at least one inaccessible biological molecule (I) in a subject comprises:

- (a) administering an isotopically labeled precursor molecule (II) so that the label becomes incorporated into (I);
- (b) recovering an accessible sample that contains at least one derivative (III) of (I), produced by in vivo metabolism, and
- (c) determining incorporation of label into (III) by mass spectrometry.

An INDEPENDENT CLAIM is also included for a kit for the new process, containing (II) and instructions.

USE - The method is useful for diagnosis of diseases associated with an altered rate of biosynthesis/breakdown of (II), specifically osteoporosis; left-ventricular hypertrophy; liver cirrhosis or fibrosis; congestive heart failure; scleroderma; coal-miner's pneumoconiosis; cardiac or lung fibrosis; Alzheimer's disease; multiple sclerosis; rheumatoid arthritis; diabetes mellitus; muscle-wasting syndromes; muscular dystrophy; athletic training and cancer. The method is also useful for monitoring response of these diseases to treatment and for determining the whole-body pool of (I) (claimed). The method is also useful for screening candidate gene or protein targets, phenotypic/human validation studies on potential drugs, drug mechanism studies and determining the risk of developing disease.

ADVANTAGE - The method does not involve invasive sampling; does not require quantitative recovery of metabolites (III), is insensitive to variations in in vivo clearance efficiency, metabolic transfer rate of storage of (III); and provides information about synthesis rate, transit time and tissue residence time as well as breakdown rate.

Dwg.0/9

L12 ANSWER 3 OF 4 USPATFULL ON STN

ACCESSION NUMBER: 2001:158263 USPATFULL
TITLE: Methods for diagnosing atherosclerosis by measuring endogenous heparin and methods for treating atherosclerosis using heparin
INVENTOR(S): Klock, John C., Nicasio, CA, United States
PATENT ASSIGNEE(S): BioMarin Pharmaceuticals, Novato, CA, United States
(U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6291439 | B1 | 20010918 |
| APPLICATION INFO.: | US 1998-145477 | | 19980902 (9) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | GRANTED | | |
| PRIMARY EXAMINER: | Warden, Jill | | |
| ASSISTANT EXAMINER: | Starsiak, Jr., John S. | | |
| LEGAL REPRESENTATIVE: | Halluin, Albert P., Bigornia, LuisaHowrey Simon Arnold & White, LLP | | |
| NUMBER OF CLAIMS: | 14 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 15 Drawing Figure(s); 12 Drawing Page(s) | | |
| LINE COUNT: | 1387 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides methods for measuring endogenous heparin in a mammal at levels that were previously undetectable. The present invention further features methods for assessing the risk for and

assessing the progression of atherosclerosis and methods for treating or inhibiting the progression of atherosclerosis. The invention also features methods for monitoring plasma heparin levels in subjects undergoing heparin treatment. Additionally, the present invention provides kits for assaying for heparin in biological samples.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:846739 CAPLUS
 DOCUMENT NUMBER: 123:225931
 TITLE: Immunomodulation using NKR-P1, CD69 and ligands therefor
 INVENTOR(S): Feizi, Ten; Bezouska, Karel
 PATENT ASSIGNEE(S): Medical Research Council, UK
 SOURCE: PCT Int. Appl., 165 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9521618 | A1 | 19950817 | WO 1995-GB321 | 19950215 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9516691 | A1 | 19950829 | AU 1995-16691 | 19950215 |
| PRIORITY APPLN. INFO.: | | | GB 1994-2890 | 19940215 |
| | | | GB 1994-12952 | 19940628 |
| | | | GB 1994-22584 | 19941109 |
| | | | WO 1995-GB321 | 19950215 |

AB Monosaccharide and oligosaccharide ligands for NKR-P1 and CD69, expressed on the surface of effector cells of the immune system, including Natural Killer (NK) cells, are identified and demonstrated to be useful in enhancing and inhibiting effector function, including cytotoxicity. Effector function is enhanced when ligands are clustered, e.g. on liposomes or engineered amino acid sequences, and inhibited when the ligands are in monomeric or free form. Ligands and/or effector cells may be targeted to target cells using members of specific binding pairs, such as antibodies. Soluble forms of NKR-P1 and CD69 may also be used. The oligosaccharide comprises glycosaminoglycan, sulfide, sulfated ganglioside other than sulfatide, 6-sialyl hexose, 3-O-sulfated uronic acid, keratan sulfate, chondroitin sulfate, **heparin sulfate**, **disaccharide**, tetrasaccharide, etc.

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 27.31 | 85.72 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -0.69 | -7.62 |

FILE 'REGISTRY' ENTERED AT 11:20:47 ON 27 APR 2004
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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 COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7
DICTIONARY FILE UPDATES: 25 APR 2004 HIGHEST RN 676591-92-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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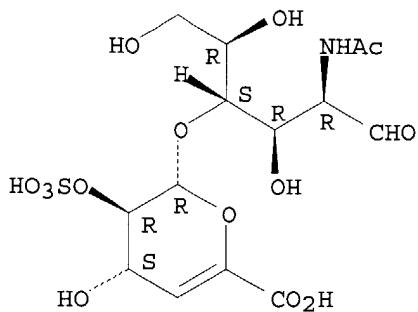
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(136098-11-8/RN)
1 136098-07-2
(136098-07-2/RN)
1 136098-08-3
(136098-08-3/RN)

L13 6 136098-05-0 OR 136098-00-5 OR 136098-04-9 OR 136098-11-8 OR 136098-07-2 OR 136098-08-3

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L13 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **136098-11-8** REGISTRY
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MF C14 H21 N O14 S . 2 Na
SR CAS Client Services
LC STN Files: CA, CAPLUS, CSChem
CRN (138706-21-5)

Absolute stereochemistry.

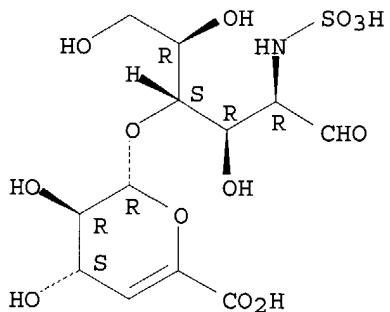


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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 136098-08-3 REGISTRY
 CN D-Glucose, 2-deoxy-4-O-(4-deoxy-alpha-L-threo-hex-4-enopyranuronosyl)-2-
 (sulfoamino)-, disodium salt (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C12 H19 N O13 S . 2 Na
 SR CAS Client Services
 LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM
 CRN (75352-09-9)

Absolute stereochemistry.

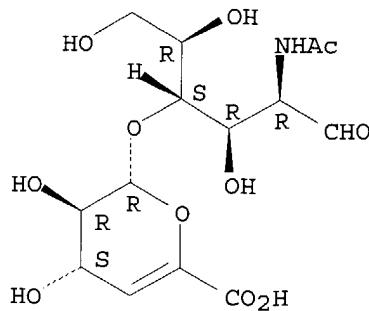


●2 Na

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 136098-07-2 REGISTRY
 CN D-Glucose, 2-(acetylamino)-2-deoxy-4-O-(4-deoxy-alpha-L-threo-hex-4-
 enopyranuronosyl)-, monosodium salt (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C14 H21 N O11 . Na
 SR CAS Client Services
 LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM
 CRN (75352-08-8)

Absolute stereochemistry.

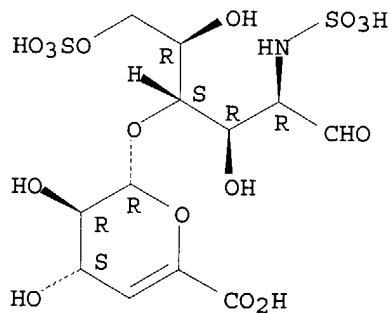


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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 136098-05-0 REGISTRY
CN D-Glucose, 2-deoxy-4-O-(4-deoxy-alpha-L-threo-hex-4-enopyranuronosyl)-2-
(sulfoamino)-, 6-(hydrogen sulfate), trisodium salt (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C12 H19 N O16 S2 . 3 Na
SR CAS Client Services
LC STN Files: CA, CAPLUS, CHEMCATS, CSCHEM
CRN (87749-24-4)

Absolute stereochemistry.

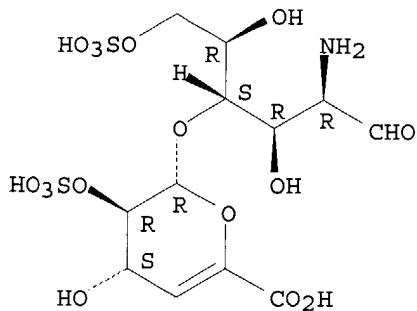


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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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RN 136098-04-9 REGISTRY
CN D-Glucose, 2-amino-2-deoxy-4-O-(4-deoxy-2-O-sulfo-alpha-L-threo-hex-4-
enopyranuronosyl)-, 6-(hydrogen sulfate), trisodium salt (9CI) (CA INDEX
NAME)
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SR CAS Client Services
LC STN Files: CA, CAPLUS, CHEMCATS
CRN (123228-41-1)

Absolute stereochemistry.

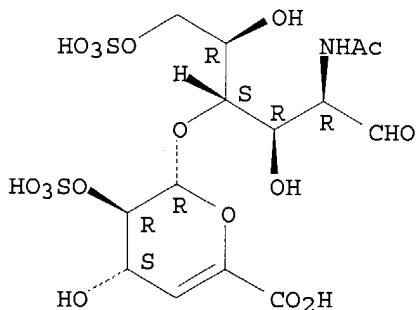


● 3 Na

1 REFERENCES IN FILE CA (1907 TO DATE)
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 RN 136098-00-5 REGISTRY
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 FS STEREOSEARCH
 MF C14 H21 N O17 S2 . 3 Na
 SR CAS Client Services
 LC STN Files: CA, CAPLUS, CSCHEM
 CRN (138706-22-6)

Absolute stereochemistry.



● 3 Na

2 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE 'STNGUIDE' ENTERED AT 10:59:22 ON 27 APR 2004

FILE 'HOME' ENTERED AT 10:59:25 ON 27 APR 2004

FILE 'REGISTRY' ENTERED AT 10:59:32 ON 27 APR 2004

L1 1 S 136098-03-8

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L4 1 S 136098-10-7

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L7 0 S 6020323/PN
L8 1 S US6020323/PN
 SEL RN

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L9 11 S E1-11

FILE 'STNGUIDE' ENTERED AT 11:15:18 ON 27 APR 2004

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, WPIDS' ENTERED AT 11:18:53 ON
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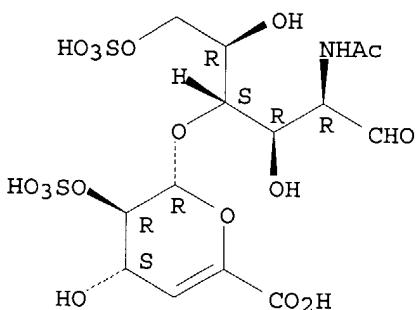
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=> d 19 tot

L9 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **138706-22-6** REGISTRY
CN D-Glucose, 2-(acetylamino)-2-deoxy-4-O-(4-deoxy-2-O-sulfo- α -L-threo-
hex-4-enopyranuronosyl)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
DR 156877-10-0, 157798-60-2, 243459-85-0, 345653-93-2
MF C14 H21 N O17 S2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

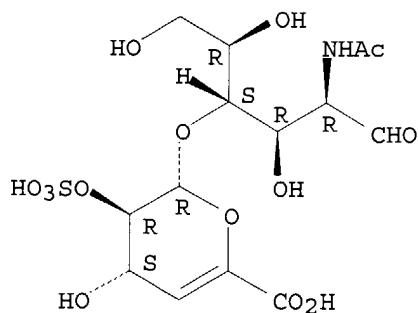


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35 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 138706-21-5 REGISTRY
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DR 151283-81-7, 156877-13-3, 157798-58-8, 243459-83-8, 345653-94-3
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

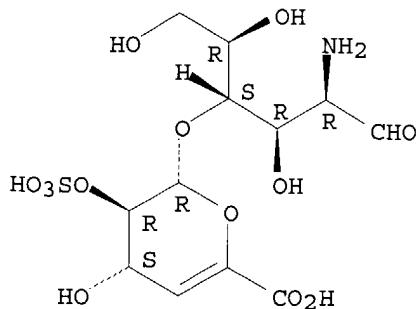


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RN 138692-82-7 REGISTRY
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DR 156877-14-4
MF C12 H19 N O13 S
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SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



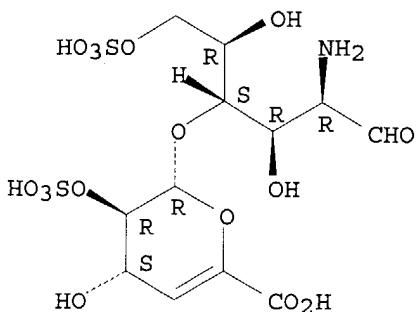
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13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **123228-41-1** REGISTRY
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Absolute stereochemistry.

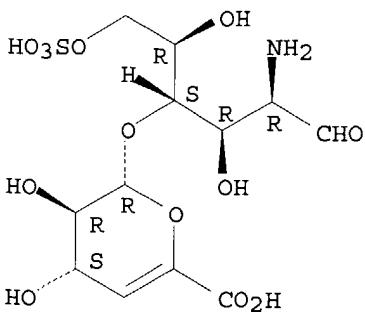


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 CI COM
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 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

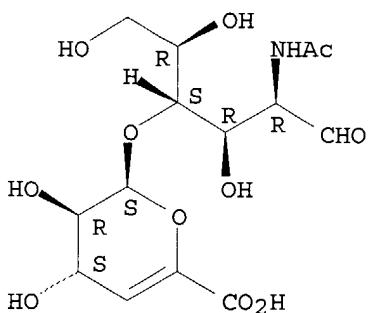


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L9 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **119603-24-6** REGISTRY
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 MF C14 H21 N O11
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 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

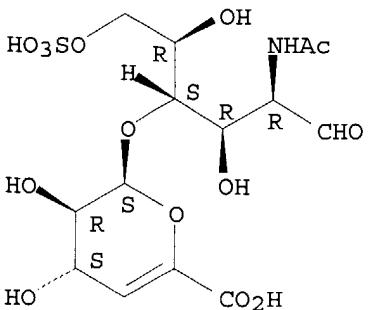


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6 REFERENCES IN FILE CA (1907 TO DATE)
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L9 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **119577-27-4** REGISTRY
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 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



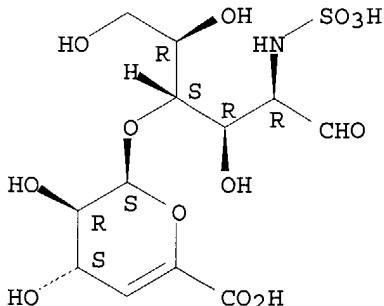
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 8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **119577-26-3** REGISTRY
 CN D-Glucose, 2-deoxy-4-O-(4-deoxy- β -L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)- (9CI) (CA INDEX NAME)

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 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

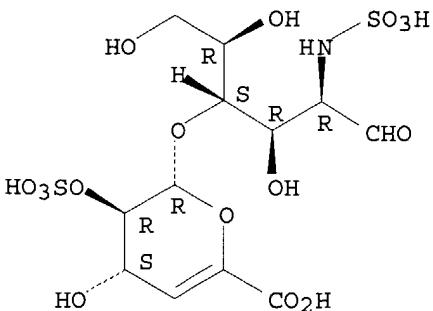
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 RN 53695-16-2 REGISTRY
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OTHER NAMES:

CN ADiH-2,N-dis
 FS STEREOSEARCH
 DR 449762-63-4, 151283-84-0, 156877-09-7, 157798-61-3, 191162-73-9,
 243459-84-9, 345653-92-1, 358753-64-7, 412024-30-7
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 CI COM
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



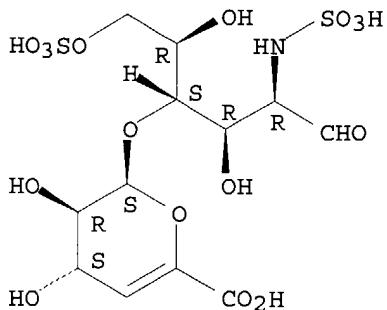
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L9 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 51449-06-0 REGISTRY
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 FS STEREOSEARCH

DR 358753-63-6
MF C12 H19 N O16 S2
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

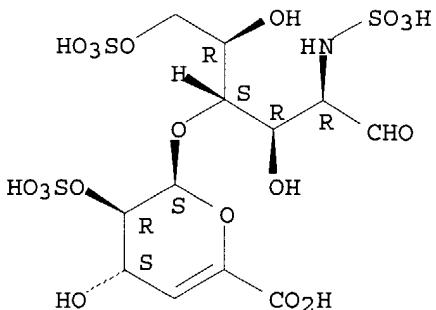


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10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN 51449-05-9 REGISTRY
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FS STEREOSEARCH
DR 152045-03-9
MF C12 H19 N O19 S3
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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|--|------------|---------|
| COST IN U.S. DOLLARS | ENTRY | SESSION |
| FULL ESTIMATED COST | 31.77 | 117.49 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| CA SUBSCRIBER PRICE | ENTRY | SESSION |
| | 0.00 | -7.62 |

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FILE 'USPATFULL' ENTERED AT 11:22:53 ON 27 APR 2004
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FILE 'WPIDS' ENTERED AT 11:22:53 ON 27 APR 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

=> s l13
L14 2 L13

=> d tibib abs tot
'TIBIB' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data and PI table (default)
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
DMAX ----- MAX, delimited for post-processing
FAM ----- AN, PI and PRAI in table, plus Patent Family data
FBIB ----- AN, BIB, plus Patent FAM
IND ----- Indexing data
IPC ----- International Patent Classifications
MAX ----- ALL, plus Patent FAM, RE
PATS ----- PI, SO
SAM ----- CC, SX, TI, ST, IT
SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
 SCAN must be entered on the same line as the DISPLAY,
 e.g., D SCAN or DISPLAY SCAN)
STD ----- BIB, IPC, and NCL

IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IMAX ----- MAX, indented with text labels
ISTD ----- STD, indented with text labels

OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

HIT ----- Fields containing hit terms
HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)
 containing hit terms
HITRN ----- HIT RN and its text modification
HITSTR ----- HIT RN, its text modification, its CA index name, and
 its structure diagram
HITSEQ ----- HIT RN, its text modification, its CA index name, its
 structure diagram, plus NTE and SEQ fields

FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC ----- Hit term plus 20 words on either side
OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):ibib

L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:116287 CAPLUS
DOCUMENT NUMBER: 139:334949
TITLE: Retention studies of sulphated glycosaminoglycan disaccharides on porous graphitic carbon capillary columns
AUTHOR(S): Koivisto, P.; Stefansson, M.
CORPORATE SOURCE: Uppsala Research Imaging Solution AB, Uppsala, 75185, Swed.
SOURCE: Chromatographia (2003), 57(1/2), 37-45
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:136668 CAPLUS
DOCUMENT NUMBER: 135:256060
TITLE: Disaccharides derived from heparin or heparan sulfate regulate IL-8 and IL-1 β secretion by intestinal epithelial cells
AUTHOR(S): Chowers, Yehuda; Lider, Ofer; Schor, Hagai; Barshack, Iris; Tal, Ruth; Ariel, Amiram; Bar-Meir, Simon; Cohen, Irun R.; Cahalon, Liora
CORPORATE SOURCE: Departments of Gastroenterology, Chaim Sheba Medical Center, Tel-HaShomer, Israel
SOURCE: Gastroenterology (2001), 120(2), 449-459
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 19
L15 84 L9

=> s blood clot or thrombo?
L16 507335 BLOOD CLOT OR THROMBO?

=> s l15 and l16
L17 3 L15 AND L16

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18 3 DUP REM L17 (0 DUPLICATES REMOVED)

=> d ibib abs tot

L18 ANSWER 1 OF 3 USPATFULL on STN
ACCESSION NUMBER: 2002:340378 USPATFULL
TITLE: Glycosaminoglycan derivatives and processes for preparing same
INVENTOR(S): Usuki, Seigou, Tokyo, JAPAN
Kariya, Yutaka, Kanagawa, JAPAN
PATENT ASSIGNEE(S): Seikagaku Corporation, Tokyo, JAPAN (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6498246 | B1 | 20021224 |
| | WO 9943714 | | 19990902 |
| APPLICATION INFO.: | US 2000-623132 | | 20000828 (9) |
| | WO 1999-JP899 | | 19990226 |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1998-60336 | 19980226 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Wilson, James O. | |
| ASSISTANT EXAMINER: | Lewis, Patrick | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 9 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 8 Drawing Figure(s); 8 Drawing Page(s) | |
| LINE COUNT: | 1052 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides novel glycosaminoglycan derivatives having a repeating unit structure of two saccharides of hexosamine and hexuronic acid as a backbone structure, in which the bonds between 2- and 3-positions carbon atoms of hexuronic acid as its constituting monosaccharide are partially cleaved and a part or all of the 2-position hydroxyl groups of uncleaved hexuronic acid are not substituted with a sulfate group, which has low anticoagulation activity and excellent neurite outgrowth promotion accelerating activity and sialidase inhibition activity; a process for producing the glycosaminoglycan derivatives, comprising a cleavage treatment of the bond between the 2- and 3-position carbon atoms of hexuronic acid having no sulfate group at the 2-position of glycosaminoglycan, and a selective desulfation treatment of the 2-position sulfate group of hexuronic acid; and a pharmaceutical composition comprising the glycosaminoglycan derivative as an active ingredient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:903377 CAPLUS
DOCUMENT NUMBER: 137:72902
TITLE: Heparin reacts with and inactivates nitric oxide
AUTHOR(S): Upchurch, Gilbert R., Jr.; Goodman, Dorinda G.; Willoughby, Scott R.; Zhang, Ying-Yi; Welch, George N.; Freedman, Jane E.; Ye, Song; Costello, Catherine E.; Loscalzo, Joseph
CORPORATE SOURCE: Whitaker Cardiovascular Institute, Boston University School of Medicine, Boston, MA, 02118, USA
SOURCE: Journal of Cardiovascular Pharmacology and Therapeutics (2001), 6(2), 163-173

CODEN: JCPTFE; ISSN: 1074-2484

PUBLISHER: Westminster Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although heparin is a well-known anticoagulant, in some cases it promotes a prothrombotic state and does so through both antibody-dependent and antibody-independent platelet activation. In this study, heparin was found to reverse the antiplatelet effect of an NO donor, S-nitroso-glutathione (SNO-Glu), with an EC₅₀ of 1.8 U/mL. UV/visible spectral anal. and the Griess assay showed that increasing heparin concns. on a dose-dependent basis eliminated acidified NO_x species. Since heparin is a heterogeneous mixture of glycosaminoglycans, the effects of six different heparin disaccharides were compared with various substitutions on the hexose rings to determine which functional group(s) of the polysaccharide interact with acidified NO_x. Among the six disaccharides tested, only types I-S and II-S had the effect, suggesting that the sulfamino-group at the C2 position of the glucosamine moiety was critical for the elimination of acidified NO_x species. Mass spectrometry expts. gave results consistent with these observations, indicating that only the I-S and II-S heparin disaccharides were modified upon treatment with NaNO₂/HCl. Neg.-ion electrospray ionization MS and tandem MS analyses of the native compds. and their deuterium-labeled analogs confirmed that the reaction products from nitrosation of these N-sulfated disaccharides had eliminated the C2-sulfamino-moiety and replaced it with methoxide derived from the solvent. Participation of the 6-sulfato-substituent appears to facilitate the elimination reaction. These data show that heparin can impair the antiplatelet properties of nitric oxide by interacting with the nitrosating species, and suggest that heparin-like glycosaminoglycans may interact with endothelium-derived nitric oxide in vivo to regulate the bioactivity of this important antiplatelet and vasorelaxant substance.

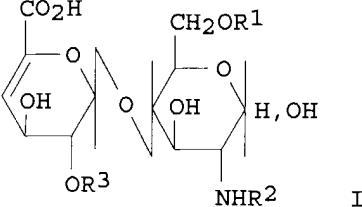
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:873298 CAPLUS
DOCUMENT NUMBER: 134:37052
TITLE: Sulfated glucosamine glycans as VEGF and neoangiogenesis inhibitors
INVENTOR(S): Ishihara, Masayuki; Ono, Katsuaki; Suzuki, Kiyoshi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2000344674 | A2 | 20001212 | JP 2000-99433 | 20000331 |
| PRIORITY APPLN. INFO.: | | | JP 1999-93472 | A 19990331 |

GI



AB Sulfated (>40 mol% S, determined by HPLC) glucosamine glycans, with repeated disaccharide unit containing glucosamine and hexuronic acid (<20 mol%) as the basic skeleton (I), and their salts are claimed as VEGF and neoangiogenesis inhibitors for treatment of neoangiogenesis-related diseases, including cancer metastasis, proliferative retinopathy, rheumatoid arthritis, ovary hyperstimulation syndrome. I induced <5% thrombin time as compare to standard heparin. Formulation examples of I injections, tablets, capsules, and ointments were given.

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=> d his

(FILE 'HOME' ENTERED AT 10:59:12 ON 27 APR 2004)

FILE 'STNGUIDE' ENTERED AT 10:59:22 ON 27 APR 2004

FILE 'HOME' ENTERED AT 10:59:25 ON 27 APR 2004

FILE 'REGISTRY' ENTERED AT 10:59:32 ON 27 APR 2004
L1 1 S 136098-03-8

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, WPIDS' ENTERED AT 11:00:27 ON
27 APR 2004
L2 4 S L1
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 11:02:55 ON 27 APR 2004
L4 1 S 136098-10-7

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, WPIDS' ENTERED AT 11:03:20 ON
27 APR 2004
L5 9 S L4
L6 9 DUP REM L5 (0 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 11:04:39 ON 27 APR 2004

FILE 'CAPLUS' ENTERED AT 11:12:14 ON 27 APR 2004
L7 0 S 6020323/PN
L8 1 S US6020323/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 11:12:45 ON 27 APR 2004
L9 11 S E1-11

FILE 'STNGUIDE' ENTERED AT 11:15:18 ON 27 APR 2004

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, WPIDS' ENTERED AT 11:18:53 ON
27 APR 2004
L10 4 S HEPARIN SULFATE DISACCHARIDE
L11 0 S HEPARIN SULFATE DISACCHARIDES
L12 4 DUP REM L10 (0 DUPLICATES REMOVED)

FILE 'REGISTRY' ENTERED AT 11:20:47 ON 27 APR 2004
L13 6 S 136098-05-0 OR 136098-00-5 OR 136098-04-9 OR 136098-11-8 OR 1

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, WPIDS' ENTERED AT 11:22:53 ON
27 APR 2004
L14 2 S L13
L15 84 S L9
L16 507335 S BLOOD CLOT OR THROMBO?
L17 3 S L15 AND L16
L18 3 DUP REM L17 (0 DUPLICATES REMOVED)

=> s cancer or neoplas? or metastasis

L19 2816564 CANCER OR NEOPLAS? OR METASTASIS

=> s l19 and l15

L20 8 L19 AND L15

=> dup rem 120

PROCESSING COMPLETED FOR L20

L21 8 DUP REM L20 (0 DUPLICATES REMOVED)

=> d ibib abs tot

L21 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:454053 CAPLUS

DOCUMENT NUMBER: 139:30781

TITLE: Heparin- and heparan sulfate-derived oligosaccharide
metastasis-blocking anticancer compounds

INVENTOR(S): Cahalon, Liora; Cohen, Irun R.; Lider, Ofer; Margalit,
Raanan

PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|---------------|----|----------|---------------|----------|
| WO 2003047501 | A2 | 20030612 | WO 2002-IL982 | 20021205 |
|---------------|----|----------|---------------|----------|

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK,
SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW, AM, AZ, BY

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

| | | | | |
|---------------|----|----------|--------------|----------|
| US 2003130230 | A1 | 20030710 | US 2001-2145 | 20011205 |
|---------------|----|----------|--------------|----------|

PRIORITY APPLN. INFO.: US 2001-2145 A 20011205

OTHER SOURCE(S): MARPAT 139:30781

AB The invention discloses a treatment for **cancer**, and in particular, therapeutic compds. which block the ability of cytokines and chemokines to promote **metastasis** of malignant cells. The therapeutic compds. comprise a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan sulfate-derived saccharide compound. In one embodiment, the carbohydrate or oligosaccharide has a mol. weight of no more than about 3000 daltons, preferably in the range of about 400-2000 daltons, most preferably between about 400-1100 daltons. Generally, substances of the invention inhibit tumor cell migration, as determined by biol. assays, and comprise mols. of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

L21 ANSWER 2 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2003:188437 USPATFULL

TITLE: Novel anti-**cancer** therapeutic compounds

INVENTOR(S): Cahalon, Liora, Givataim, ISRAEL

Cohen, Irun R., Rehovot, ISRAEL

Lider, Ofer, Kfar Bilu Bet, ISRAEL

Margalit, Raanan, Ganei Yochanan, ISRAEL

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003130230 | A1 | 20030710 |
| APPLICATION INFO.: | US 2001-2145 | A1 | 20011205 (10) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | C/O THE POLKINGHORNS, 9003 FLORIN WAY, UPPER MARLBORO, MD, 20772 | | |
| NUMBER OF CLAIMS: | 32 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 15 Drawing Page(s) | | |
| LINE COUNT: | 940 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A treatment for **cancer**, and in particular, of therapeutic compounds which block the ability of cytokines and chemokines to promote **metastasis** of malignant cells. The therapeutic compound comprises a carboxylated and/or sulfated oligosaccharide, preferably in a substantially purified form, which is a heparin or heparan-sulfate derived saccharide compound. In one embodiment of the present invention, the carbohydrate or oligosaccharide has a molecular weight of no more than about 3000 daltons, preferably lying in the range of about 400 to about 2000 daltons, most preferably between about 400 and about 1100 daltons. Generally, substances of the present invention inhibit tumor cell migration, as determined by biological assays, and comprise molecules of various sugar units of which the basic unit of activity is associated with a disaccharide. However, larger oligosaccharide chains of up to about 10 sugar units, containing the basic disaccharide unit of activity can also function to inhibit such activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:763910 CAPLUS
 DOCUMENT NUMBER: 139:258948
 TITLE: Heparin-derived disaccharides modulate proliferation and ERB-b2-mediated signal transduction in colon **cancer** cell lines. [Erratum to document cited in CA137:45011]
 AUTHOR(S): Fishman, Sigal; Brill, Shlomo; Papa, Moshe; Halpern, Zamir; Zvibel, Isabel
 CORPORATE SOURCE: Liver Metastasis Research Group, Tel Aviv Sourasky Medical Center, Gastroenterology Institute, Tel Aviv-Jaffa, Israel
 SOURCE: International Journal of Cancer (2002), 101(6), 600
 CODEN: IJCNAW; ISSN: 0020-7136
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The legend for Figure 4 contains an error. The following should be noted when looking at the figure: the control is represented by black squares and the disaccharide 9267 is represented by black circles.

L21 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:298803 CAPLUS
 DOCUMENT NUMBER: 137:45011
 TITLE: Heparin-derived disaccharides modulate proliferation and ERB-B2-mediated signal transduction in colon **cancer** cell lines
 AUTHOR(S): Fishman, Sigal; Brill, Shlomo; Papa, Moshe; Halpern, Zamir; Zvibel, Isabel
 CORPORATE SOURCE: Liver Metastasis Research Group, Tel Aviv Sourasky Medical Center, Gastroenterology Institute, Tel Aviv-Jaffa, Israel
 SOURCE: International Journal of Cancer (2002), 99(2), 179-184

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Organ-specific extracellular matrix (ECM) dets. **metastasis** formation by regulating tumor cell proliferation. Hepatocyte-derived ECM enhances proliferation of colon **cancer** cell lines by increasing expression of tyrosine kinase receptors of the erb-B family. The active components in the ECM are the heparan sulfates, which are highly heterogeneous in their chemical and size. We determined the effect of heparan sulfate disaccharides, of defined chemical and present in high amts. in the liver heparan sulfate chains, on the proliferation of colon **cancer** cell lines and investigated the mechanism involved. The low-metastatic cell line KM12 was stimulated to proliferate by a highly sulfated disaccharide, found in the highest amts. in hepatocyte-derived heparan sulfate. Growth of the highly metastatic cell line KM12SM was inhibited by the second most common disaccharide in hepatocyte-derived heparan sulfate. The effect of both disaccharides was not accompanied by changes in the expression of erb-B1, erb-B2, erb-B3 or heregulin- α . We determined whether the disaccharides modified the signal-transduction pathways mediated by the erb-B receptors. The erb-B2-specific tyrosine kinase inhibitor AG825 abolished the enhancement of KM12 cell proliferation by the stimulatory disaccharide. This disaccharide increased tyrosine phosphorylation of erb-B1 and erb-B2 receptors, effects that were abolished by AG825. Moreover, the disaccharide caused increased expression of cyclin D1 and of activated MAP kinase, again reduced in the presence of the inhibitor AG825. The growth-inhibitory disaccharide reduced phosphorylation of erb-B1, but not of erb-B2, receptors in KM12SM cells. In conclusion, not only hepatocyte-derived heparan sulfate but also disaccharide mols. derived from heparan sulfate can affect colon **cancer** cell proliferation. Their effect is mediated by modulation of the erb-B signal transduction.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:873298 CAPLUS

DOCUMENT NUMBER: 134:37052

TITLE: Sulfated glucosamine glycans as VEGF and neoangiogenesis inhibitors

INVENTOR(S): Ishihara, Masayuki; Ono, Katsuaki; Suzuki, Kiyoshi

PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

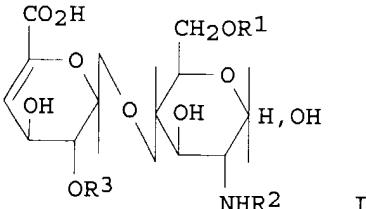
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2000344674 | A2 | 20001212 | JP 2000-99433 | 20000331 |
| PRIORITY APPLN. INFO.: | | | JP 1999-93472 | A 19990331 |

GI



AB Sulfated (>40 mol% S, determined by HPLC) glucosamine glycans, with repeated disaccharide unit containing glucosamine and hexuronic acid (<20 mol%) as the basic skeleton (I), and their salts are claimed as VEGF and neoangiogenesis inhibitors for treatment of neoangiogenesis-related diseases, including **cancer metastasis**, proliferative retinopathy, rheumatoid arthritis, ovary hyperstimulation syndrome. I induced <5% thrombin time as compare to standard heparin. Formulation examples of I injections, tablets, capsules, and ointments were given.

L21 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:227630 CAPLUS
DOCUMENT NUMBER: 124:286950
TITLE: Oligosaccharide ligands for NKR-P1 protein activate NK cells and cytotoxicity. [Erratum to document cited in CA122:7881]
AUTHOR(S): Bezouska, Karel; Yuen, Chun-Ting; O'Brien, Jacqui; Childs, Robert A.; Chai, Wengang; Lawson, Alexander M.; Drbal, Karel; Fiserova, Anna; Pospisil, Miloslav; Feizi, Ten
CORPORATE SOURCE: UK
SOURCE: Nature (London) (1996), 380(6574), 559
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstract or the index entries.

L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:209515 CAPLUS
DOCUMENT NUMBER: 122:7881
TITLE: Oligosaccharide ligands for NKR-P1 protein activate NK cells and cytotoxicity
AUTHOR(S): Bezouska, Karel; Yuen, Chun-Ting; O'Brien, Jacqui; Childs, Robert A.; Chai, Wengang; Lawson, Alexander M.; Drbal, Karel; Fiserova, Anna; Pospisil, Miloslav; Feizi, Ten
CORPORATE SOURCE: Glycosciences Lab., Northwick Park Hosp., Harrow/Middlesex, HA1 3UJ, UK
SOURCE: Nature (London) (1994), 372(6502), 150-7
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A diversity of high-affinity oligosaccharide ligands are identified for NKR-P1, a membrane protein on natural killer (NK) cells which contains an extracellular Ca²⁺-dependent lectin domain. Interactions of such oligosaccharides on the target cell surface with NKR-P1 on the killer cell surface are crucial both for target cell recognition and for delivery of stimulatory or inhibitory signals linked to the NK cytolytic machinery. NK-resistant tumor cells are rendered susceptible by preincubation with liposomes expressing NKR-P1 ligands, suggesting that purging of tumor or virally infected cells *in vivo* may be a therapeutic possibility.

L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:649336 CAPLUS
DOCUMENT NUMBER: 117:249336
TITLE: Structural differences between heparan sulfates of proteoglycan involved in the formation of basement membranes *in vivo* by Lewis-lung-carcinoma-derived cloned cells with different metastatic potentials
AUTHOR(S): Nakanishi, Hayao; Oguri, Kayoko; Yoshida, Keiichi; Itano, Naoki; Takenaga, Keizo; Kazama, Takashi; Yoshida, Aichi; Okayama, Minoru

CORPORATE SOURCE: Clin. Res. Inst., Natl. Nagoya Hosp., Nagoya, 460,
 Japan
 SOURCE: Biochemical Journal (1992), 288(1), 215-24
 CODEN: BIJOAK; ISSN: 0306-3275
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB This study addresses the characterization of heparan sulfates of the basement-membrane proteoglycans in tumor formed after the s.c. implantation of Lewis-lung-carcinoma-derived different metastatic clones (P29, LM12-3 and LM60-D6 clones with low, medium and high metastatic potentials resp.). Heparan sulfate proteoglycans (125-158 µg of hexuronate/g dry weight of tissue) were isolated from chondroitin ABC lyase digests of a proteoglycan fraction obtained after DEAE-Sephadex chromatog. of tissue exts. The proteoglycans were separated into three mol. species by Sepharose CL-4B chromatog. followed by CsCl-d.-gradient centrifugation: large proteoglycans with an estimated Mr of 820,000-130,000, which consisted of two components with low (<1.34 g/mL; PGII-M) and high (>1.37 g/mL; PGII-B) d., and a small proteoglycan with an Mr of less than 80,000 (PGIII). Of these, only the PGII-M proteoglycan (34-37 µg of hexuronate/g drug weight) reacted with the antiserum against proteoglycan of Engelbreth-Holm-Swarm-tumor basement membrane, and represented, therefore, a basement-membrane proteoglycan. Digestion with heparan sulfate lyases I and II of the heparan sulfates (/Mr 360,000) from the PGII-M proteoglycan of the three tumors resulted in almost complete depolymer. to give six unsatd. disaccharides identified as 2-acetamido-2-deoxy-4-O-(4-deoxy- α -L-threo-hex-4-enopyranosyluronic acid)-D-glucose, 2-acetamido-2-deoxy-4-O-(4-deoxy- α -threo-hex-4-enopyranosyluronic acid)-6-O-sulfo-D-glucose, 2-deoxy-2-sulfamino-4-O-(4-deoxy- α -L-threo-hex-4-enopyranosyluronic acid)-D-glucose, 2-deoxy-2-sulfamino-4-O-(4-deoxy- α -L-threo-hex-4-enopyranosyluronic acid)-6-O-sulfo-D-glucose, 2-deoxy-2-sulfamino-4-O-(4-deoxy-2-O-sulfo- α -L-threo-hex-4-enopyranosyluronic acid)-D-glucose and 2-deoxy-2-sulfamino-4-O-(4-deoxy-2-O-sulfo- α -L-threo-hex-4-enopyranosyluronic acid)-6-O-sulfo-D-glucose. Comparison of the relative amts. of these disaccharides produced from the three tumor-derived heparan sulfates demonstrated that the degree of sulfation of the heparan sulfates correlated with the degree of morphol. organization of the tumor basement membranes; the heparan sulfate from the more highly metastatic tumor with more highly organized basement membrane exhibited a higher degree of overall sulfation along the glycosaminoglycan chains, which was due to an increased content of the three repeating disaccharides having 6-O-sulfated glucosamine residues.

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